UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

ABBOTT LABORATORIES, an Illinois corporation, Plaintiff, v. TEVA PHARMACEUTICALS USA, INC., a Delaware corporation, Defendant.	Civil Action No.

COMPLAINT

Plaintiff Abbott Laboratories ("Abbott"), for its complaint against defendant Teva Pharmaceuticals USA, Inc. ("Teva"), alleges as follows:

THE PARTIES

1. Abbott is a corporation organized under the laws of the State of Illinois, having its headquarters and principal place of business at Abbott Park, Illinois 60064.

2. Teva is a corporation organized under the laws of the State of Delaware, having its principal place of business at 1090 Horsham Rd., P.O. Box 1090, North Wales, Pennsylvania 19454.

JURISDICTION AND VENUE

3. This Court has subject matter jurisdiction over this suit pursuant to 28 U.S.C. § 1331 and § 1338(a), as it arises under an Act of Congress relating to patents, Title 35, United States Code, §§ 1, *et seq.* Specifically, this action arises under the Hatch-Waxman Act, 35 U.S.C. § 271(e)(2).

4. This Court has personal jurisdiction over Teva because, among other things, Teva is a Delaware corporation.

5. Venue properly exists in this judicial district pursuant to 28 U.S.C. § 1391 and § 1400(b).

FACTUAL BACKGROUND

The '953 Patent

6. Abbott sells a prescription drug product under the trademark DEPAKOTE®, which product is indicated for the treatment of epileptic seizures or convulsions, bipolar disease, and migraine headaches. The active ingredient in DEPAKOTE® is divalproex sodium.

7. On August 4, 2000, the United States Food and Drug Administration ("FDA") approved Abbott's New Drug Application No. 21-168 to market DEPAKOTE® ER (extended-release) tablets in a 500 mg dosage strength. As a result, DEPAKOTE® ER is included in the FDA's list of "Approved Drug Products With Therapeutic Equivalence Evaluations," also known as the "Orange Book." Approved drugs listed in the Orange Book may be used as the basis of a later applicant's Abbreviated New Drug Application to obtain approval of the applicant's generic drug product under the provisions of 21 U.S.C. § 355(j).

8. United States Patent No. 6,419,953 ("the '953 patent"), titled Controlled Release Formulation of Divalproex Sodium, issued on July 16, 2002. (A copy of the '953 patent is attached as Exhibit A.) The '953 patent expires December 18, 2018.

9. Abbott is the owner of and has the right to enforce the '953 patent.

10. The '953 patent is listed in the FDA's Orange Book in association with DEPAKOTE® ER.

Teva Notifies Abbott Regarding the Filing of ANDA No. 78-700

11. Abbott received a letter from Teva, dated March 20, 2007, which stated that (i) Teva had submitted Abbreviated New Drug Application No. 78-700 (the "ANDA") to the FDA, requesting approval to market a generic version of DEPAKOTE® ER – called "Divalproex

Sodium Extended Release Tablets" – in a 500 mg dosage strength; (ii) the ANDA included a Paragraph IV Certification (21 U.S.C. § 355(j)(2)(A)(vii)(IV)) directed to the '953 patent; and (iii) Teva seeks FDA approval to market its proposed generic product before the '953 patent expires.

12. Teva attached to its March 20, 2007 letter a purportedly "Detailed Statement of the Factual and Legal Bases" for the Paragraph IV Certification with regards to the '953 patent. *See* 21 U.S.C. § 355(j)(2)(B)(iv); *see also* 21 C.F.R. § 314.95(c)(6)(i) - (ii). Teva stated its position in that document regarding whether its proposed product would infringe the '953 patent, but did not argue that the '953 patent is either invalid or unenforceable.

13. The active ingredient in Teva's proposed generic drug product is divalproex sodium, and the ANDA purports to describe a formulation for achieving a controlled-release formulation of divalproex sodium in patients.

COUNT I: INFRINGEMENT OF THE '953 PATENT

14. Abbott repeats and incorporates by reference each and every allegation of paragraphs 1-13 as if fully set forth herein.

15. Under 35 U.S.C. § 271(e)(2), the submission of an ANDA under 21 U.S.C. § 355(j) for a drug claimed in a patent or for a drug use claimed in a patent is an act of infringement if the applicant seeks FDA marketing approval effective prior to the expiration of the patent. Teva's submission of ANDA No. 78-700 for approval to sell Divalproex Sodium Extended Release Tablets in a 500 mg dosage strength before the expiration of the '953 patent constitutes an act of infringement of that patent pursuant to 35 U.S.C. § 271(e)(2).

16. Teva's proposed generic version of DEPAKOTE® ER utilizes a controlled-release formulation that infringes the '953 patent.

17. Abbott has no adequate remedy at law to redress Teva's infringement.

PRAYER FOR RELIEF

WHEREFORE, Abbott prays for the following relief:

a. a judgment that the '953 patent is infringed under 35 U.S.C. § 271(e)(2) by the filing of ANDA No. 78-700;

b. an order declaring that ANDA No. 78-700 cannot be approved earlier than the expiration date of Abbott's '953 patent;

c. an injunction preventing Teva, or any of its affiliates, from commercially manufacturing, selling, offering to sell, importing, or using the product described in ANDA No. 78-700, or otherwise infringing one or more claims of the '953 patent during the life of the patent;

d. an award of Abbott's costs and attorneys' fees pursuant to 35 U.S.C. § 271(e)(4) and § 285; and

e. such other and further relief as this Court may deem just and proper.

Dated: May 4, 2007

Respectfully submitted,

CONNOLLY BOVE LODGE & HUTZ LLP

By: _____

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CERTIFICATE OF SERVICE

The undersigned, an attorney, hereby certifies that, on May 4, 2007, the foregoing **Complaint** was served on the person(s) listed below via email and U.S. Mail, postage pre-paid:

John North
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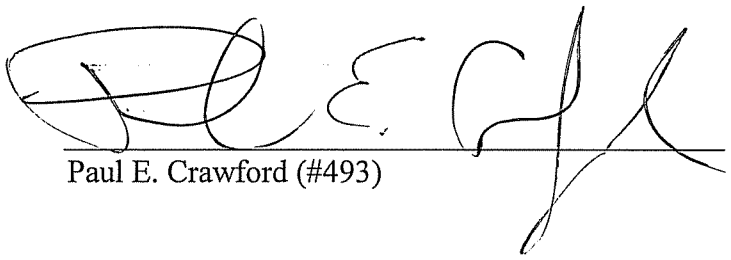

Paul E. Crawford (#493)

UNITED STATES DISTRICT COURT FOR THE DISTRICT OF DELAWARE

ABBOTT LABORATORIES, an Illinois corporation, Plaintiff, v. TEVA PHARMACEUTICALS USA, INC., a Delaware corporation, Defendant.	Civil Action No.

PLAINTIFF ABBOTT LABORATORIES' CORPORATE DISCLOSURE STATEMENT

Pursuant to Federal Rule of Civil Procedure 7.1, Plaintiff Abbott Laboratories states that it has no parent corporation and no publicly held corporation owns ten percent or more of Abbott Laboratories' stock.

Dated: May 4, 2007

Respectfully submitted,

CONNOLLY BOVE LODGE & HUTZ LLP

By: _____

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CERTIFICATE OF SERVICE

The undersigned, an attorney, hereby certifies that, on May 4, 2007, the foregoing **Plaintiff Abbott Laboratories' Corporate Disclosure Statement** was served on the person(s) listed below via email and U.S. Mail, postage pre-paid:

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Paul E. Crawford (#493)

Exhibit A

US006419953B1

(12) **United States Patent**
Qiu et al.

(10) **Patent No.: US 6,419,953 B1**
(45) **Date of Patent: *Jul. 16, 2002**

(54) **CONTROLLED RELEASE FORMULATION OF DIVALPROEX SODIUM**

(75) Inventors: **Yihong Qiu**, Gurnee; **Paul Richard Poska**, Mundelein; **Howard S. Cheskin**, Glencoe; **J. Daniel Bollinger**, Libertyville, all of IL (US); **Robert K. Engh**, Kenosha, WI (US)

(73) Assignee: **Abbott Laboratories**, Abbott Park, IL (US)

(*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/216,650**

(22) Filed: **Dec. 18, 1998**

(51) **Int. Cl.**[7] **A61K 9/20**; A61K 9/14; A61K 9/50; A61K 9/26

(52) **U.S. Cl.** **424/465**; 424/464; 424/489; 424/499; 424/468; 424/470

(58) **Field of Search** 424/489, 497, 424/470, 473, 468, 464, 465, 499

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,369,172	A	1/1983	Schor et al.	
4,913,906	A	4/1990	Friedman et al.	
4,988,731	A	1/1991	Meade	
5,009,897	A	4/1991	Brinker et al.	
5,017,613	A	5/1991	Aubert et al.	
5,019,398	A	5/1991	Daste	
5,055,306	A	10/1991	Barry et al.	
5,169,642	A	12/1992	Brinker et al.	
5,185,159	A	2/1993	Aubert et al.	
5,212,326	A	5/1993	Meade	
5,589,191	A	12/1996	Ukigaya et al.	
5,980,913	A	* 11/1999	Ayer et al.	424/470
6,077,542	A	6/2000	Sherman	
6,150,410	A	11/2000	Engh et al.	

FOREIGN PATENT DOCUMENTS

EP	0 141 267	B1	8/1987
EP	0 430 287	B2	6/1991
EP	WO 98/47491	*	10/1998
WO	WO 94/27587		8/1994
WO	98/47491		10/1998
WO	WO 00/45793	A1	8/2000

OTHER PUBLICATIONS

"Metabolism of Antiepileptic Drugs", 143–151, R.H. Levey, Ed., Raven Press, New York (1984).
Bialer et al., *Int. J. Pharmaceutics*, 20: 53–63 (1984).
Bialer et al., *Biopharmaceutics and Drug Disposition*, 6: 401–411 (1985).

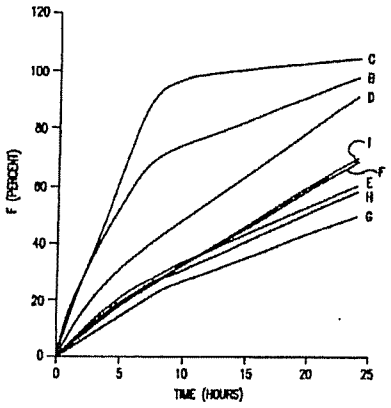
(List continued on next page.)

Primary Examiner—Thurman K. Page
Assistant Examiner—Isis Ghali
(74) *Attorney, Agent, or Firm*—James D. McNeil

(57) **ABSTRACT**

The present invention pertains to a hydrophilic matrix tablet suitable for the once-a-day administration of valproate compounds such as divalproex sodium. The tablet comprises from about 50 weight percent to about 55 weight percent of an active ingredient selected from the group consisting of valproic acid, a pharmaceutically acceptable salt or ester of valproic acid, divalproex sodium, and valpromide; from about 20 weight percent to about 40 weight percent hydroxypropyl methylcellulose; from about 5 weight percent to about 15 weight percent lactose, from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 weight percent to about 5 weight percent of silicon dioxide; all weight percentages based upon the total weight of the tablet dosage form. Other aspects of the invention relate to the use of this formulation in the treatment of epilepsy and to methods for manufacturing this dosage form.

16 Claims, 4 Drawing Sheets



OTHER PUBLICATIONS

Abstract of Wilder, et al., "Twice–daily Dosing of Valproate with Divalproex", Clinical Pharmacology and Therapeutics, United States, 1983, 34/4 (501–504).

Freitag, et al., "Depakote ER in Migraine Prophylaxis", Abstract No. S07.003, Nuerology 54 Apr. 2000 (Suppl 3), p. A14.

Collins, et al., "Depakote CR: Biopharmaceutical and Pharmacokinetic Studies of a New Formulation for Once Daily Dosing", Neurology, vol. 50(4), Supplement 4, Apr. 1998, p. A426.

Samara, et al., "Bioavailability of a Controlled–Release Formulation of Depakote", No. 3.053, Epilepsia, vol. 38, Suppl. 8, 1997.

Cavanaugh, et al., "Effect of Food on the Bioavailability of a Controlled Release Formulation of Depakote Under Multiple Dose Conditions", No. 2.002, Epilepsia, vol. 38, Suppl. 8, 1997.

Physicians' Desk Reference, 54th Edition, 2000, Depakene Capsules, pp. 426–427, published by Medical Economics Company, Inc.

Physicians' Desk Reference, 54th Edition, 2000, Depakote Tablets, pp. 431–437, published by Medical Economics Company, Inc.

* cited by examiner

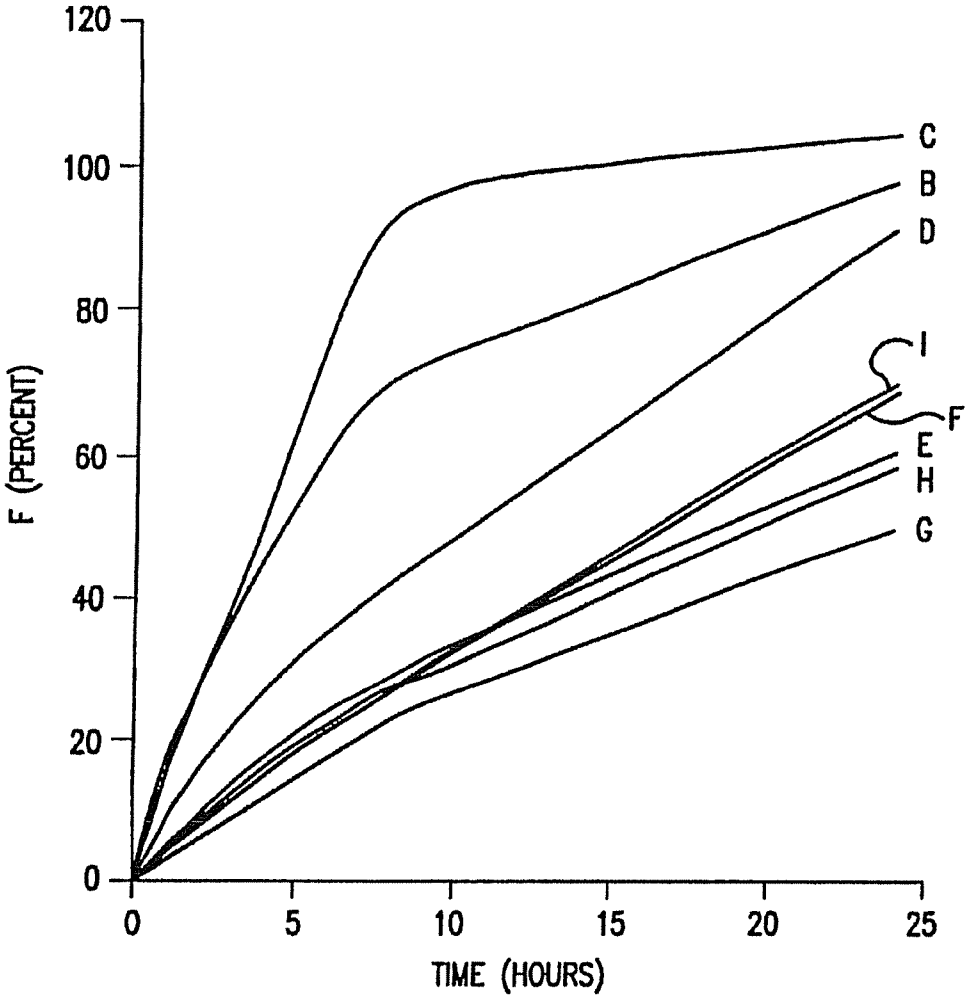

120
100
80
60
40
20
0
F (PERCENT)
0
5
10
15
20
25
TIME (HOURS)
C
B
D
I
F
E
H
G

FIG. 1

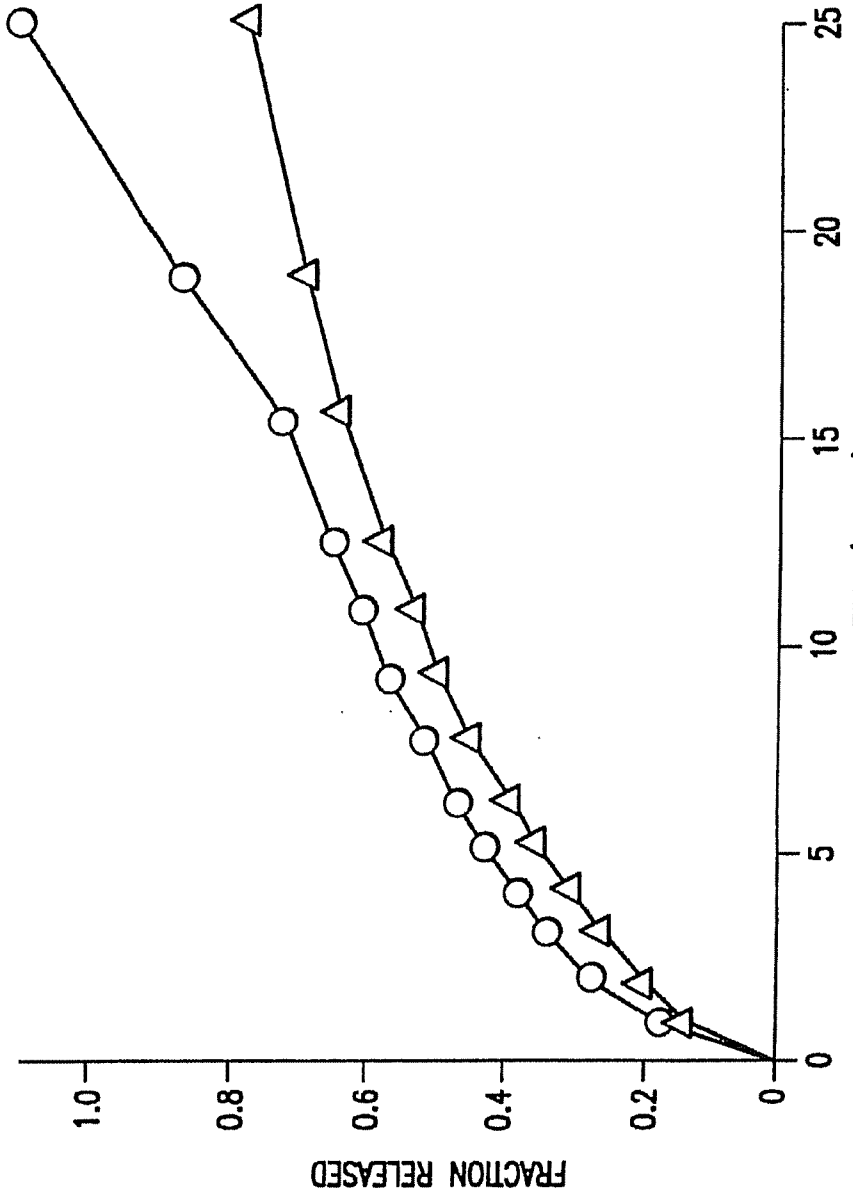


FIG.2

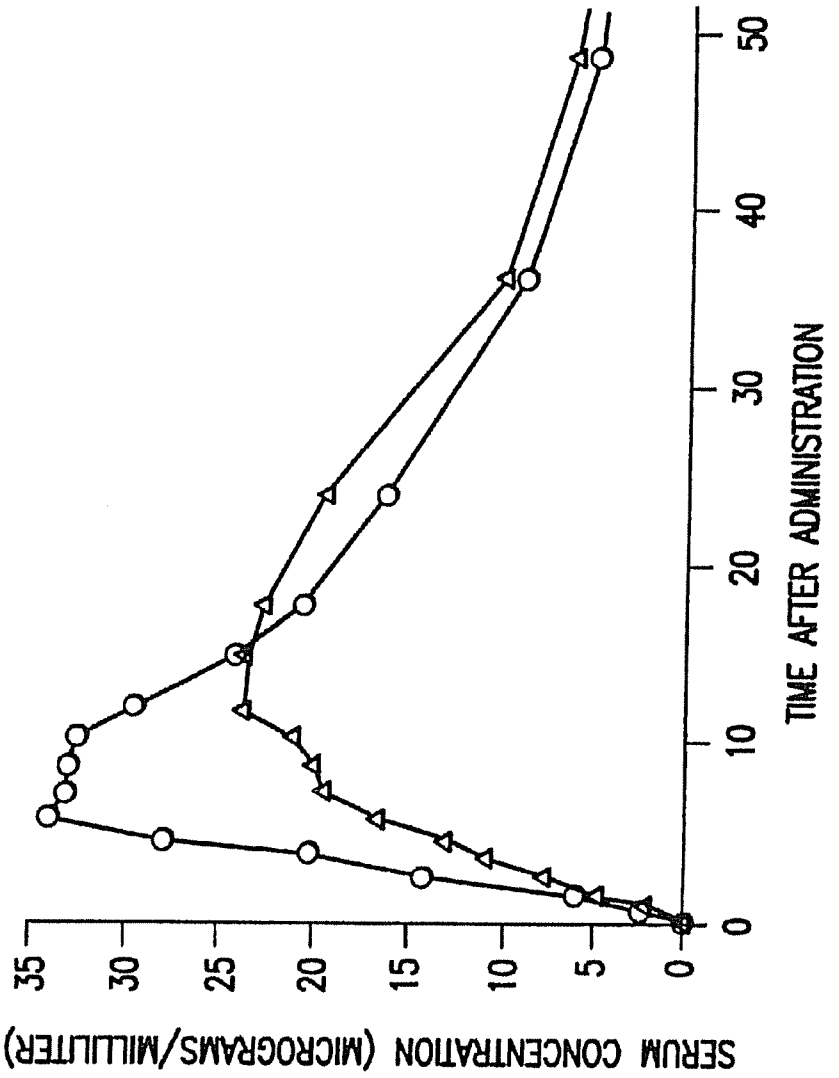

SERUM CONCENTRATION (MICROGRAMS/MILLILITER)
35
30
25
20
15
10
5
0
0
10
20
30
40
50
TIME AFTER ADMINISTRATION

FIG.3

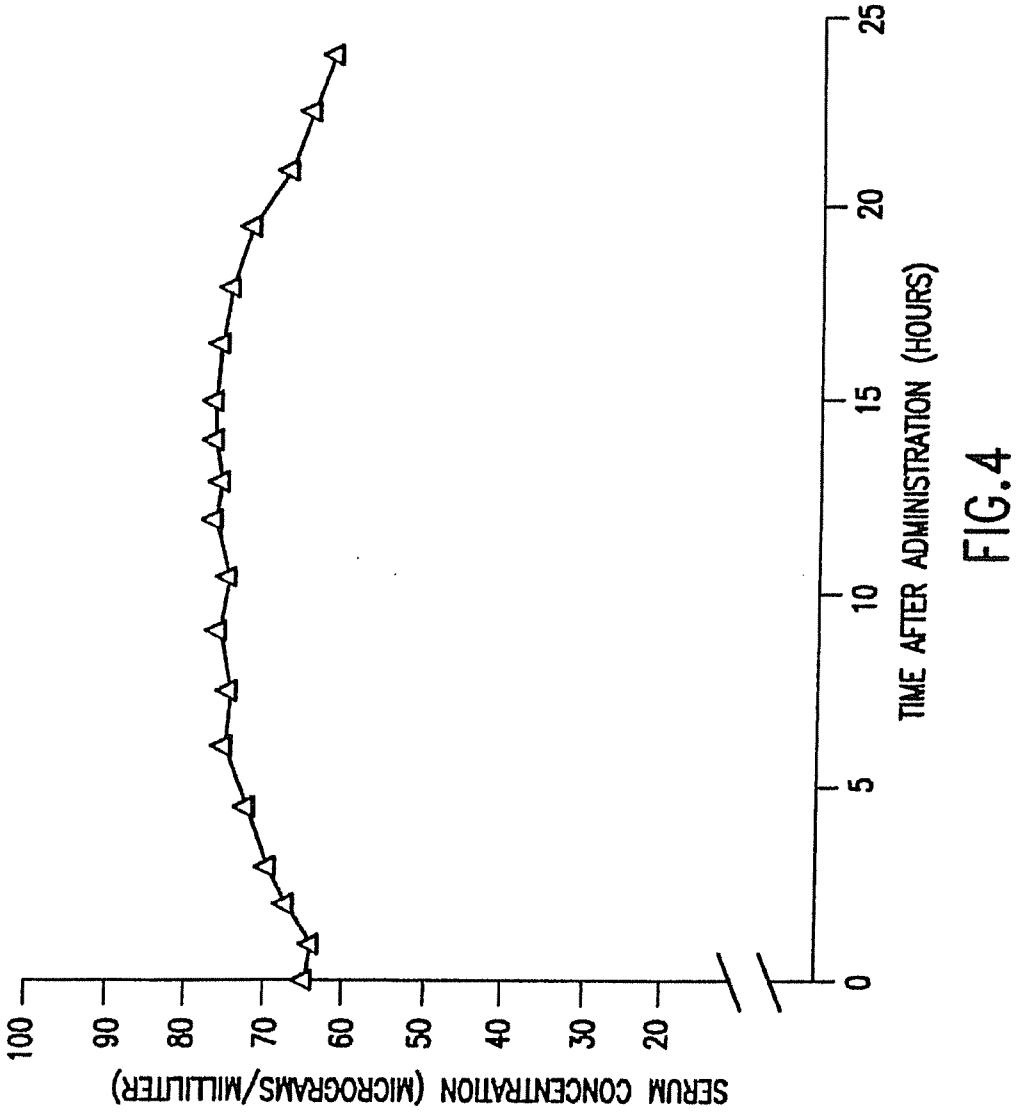

SERUM CONCENTRATION (MICROGRAMS/MILLILITER)
100
90
80
70
60
50
40
30
20
0
5
10
15
20
25
TIME AFTER ADMINISTRATION (HOURS)

FIG.4

CONTROLLED RELEASE FORMULATION OF DIVALPROEX SODIUM

TECHNICAL FIELD

The present invention relates to pharmaceutical formulations. More particularly, the present invention concerns a formulation comprising valproic acid, a pharmaceutically acceptable salt, ester, or amide thereof or divalproex sodium, in a controlled release tablet formulation.

BACKGROUND OF THE INVENTION

2-Propylpentanoic acid, more commonly known as valproic acid (VPA), its amide, valpromide (VPO), and certain salts and esters of the acid are effective in the treatment of epileptic seizures or as antipsychotic agents. U.S. Pat. No. 4,988,731 to Meade discloses an oligomer having a 1:1 molar ratio of sodium valproate and valproic acid containing 4 units, and U.S. Pat. 5,212,326 to Meade discloses a stable, non-hygroscopic solid form of valproic acid which comprises an oligomer having 1:1 molar ratio of sodium valproate and valproic acid and containing four to six units. Divalproex sodium (sodium hydrogen divalproate) is one of the most widely accepted antiepileptic agents currently available.

However, despite its efficacy in the treatment of epilepsy, valproic acid has been shown to exhibit an elimination half-life which is shorter than other commonly used antiepileptic agents. Half-lives for the drug of between six and seventeen hours in adults and between four and fourteen hours in children have been reported. This leads to substantial fluctuations in the plasma concentration of the drug, especially in chronic administration. To maintain reasonably stable plasma concentrations, it is necessary to resort to frequent dosing, and the resulting inconvenience to the patient often results in lowered compliance with the prescribed dosing regimen. Moreover, widely fluctuating plasma concentrations of the drug may result in administration of less than therapeutic amounts of the drug in a conservative dosing regimen, or amounts too large for the particular patient in an aggressive dosing regimen.

To overcome this disadvantage, a concerted effort has been devoted to the discovery of valproic acid formulations which will maintain more constant plasma levels of the drug following administration. The ultimate goal of these studies has been the discovery of a formulation which affords stable plasma levels in a once-a-day dosing regimen. These efforts fall generally into one of two categories: (a) finding a form of the active ingredient which is more slowly released to the body metabolically, and (b) finding a formulation which delivers the drug by either a timed- or controlled-release mechanism.

U.S. Pat. No. 4,369,172 to Schor, et al. describes, for example, a prolonged release therapeutic composition based on mixtures of hydroxypropyl methylcellulose, ethyl cellulose and/or sodium carboxymethyl cellulose. The patentees provide a long list of therapeutic agents which they suggest can be incorporated into the formulation including sodium valproate.

U.S. Pat. No. 4,913,906 to Friedman, et al. discloses a controlled release dosage form of valproic acid, its amide, or one of its salts or esters in combination with a natural or synthetic polymer, pressed into a tablet under high pressure.

U.S. Pat. No. 5,009,897 to Brinker, et al. discloses granules, suitable for pressing into tablets, the granules comprising a core of divalproex sodium and a coating of a mixture of a polymer and microcrystalline cellulose.

U.S. Pat. No. 5,019,398 to Daste discloses a sustained-release tablet of divalproex sodium in a matrix of hydroxypropyl methylcellulose and hydrated silica.

U.S. Pat. No. 5,055,306 to Barry, et al. discloses an effervescent or water-dispersible granular sustained release formulation suitable for use with a variety of therapeutic agents. The granules comprise a core comprising the active ingredient and at least one excipient, and a water insoluble, water-swellable coating comprising a copolymer of ethyl acrylate and methyl methacrylate and a water soluble hydroxylated cellulose derivative. The patentees suggest a list of therapeutic agents which may be used in the formulation of the invention, including sodium valproate.

U.S. Pat. No. 5,169,642 to Brinkler, et al. discloses a sustained release dosage form comprising granules of divalproex sodium or amides or esters of valproic acid coated with a sustained release composition comprising ethyl cellulose or a methacrylic methyl ester, a plasticizer, a detackifying agent, and a slow-release polymeric viscosity agent.

U.S. Pat. No. 5,185,159 to Aubert, et al. discloses a formulation of valproic acid and sodium valproate which is prepared without the use of either a binder or a granulating solvent. The formulation optionally contains precipitated silica as an anti-sticking or detackifying agent.

U.S. Pat. No. 5,589,191 to Exigua, et al. discloses a slow release sodium valproate tablet formulation in which the tablets are coated with ethyl cellulose containing silicic acid anhydride.

Published PCT application WO 94/27587 to Ayer, et al. discloses a method for control of epilepsy by delivering a therapeutic composition of valproic acid or a derivative in combination with a poly(alkylene oxide).

Bialer, et al., "Metabolism of Antiepileptic Drugs," pp. 143–151, R. H. Levy, Ed., Raven Press, New York, 1984; *Int. J. Pharmaceutics,* 20: 53–63 (1984); and *Biopharmaceutics and Drug Disposition,* 6: 401–411 (1985); and *Israel J. Med. Sci.,* 20: 46–49 (1995) report the pharmacokinetic evaluation of several sustained release formulations of valproic acid.

There remains, however, the need for a sustained release formulation of valproic acid which will effectively maintain plasma concentrations of the drug at more constant levels.

SUMMARY OF THE INVENTION

The present invention provides, in its principal embodiment, a controlled release tablet dosage form comprising from about 50 weight percent to about 55 weight percent of an active ingredient selected from the group consisting of valproic acid, a pharmaceutically acceptable salt or ester of valproic acid, divalproex sodium, and valpromide; from about 20 weight percent to about 40 weight percent hydroxypropyl methylcellulose; from about 5 weight percent to about 15 weight percent lactose, from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 weight percent to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 microns; all weight percentages based upon the total weight of the tablet dosage form.

The tablet provides the active pharmaceutical in a hydrophilic matrix which slowly releases the active agent over a prolonged period of time in such a manner as to provide substantially level plasma concentrations of the drug following once-a-day dosing.

In an alternative embodiment, the present invention provides a dry granular composition suitable for compressing

into a tablet dosage form, the granular composition comprising particles of a size smaller than about I mm comprising from about 50 weight percent to about 55 weight percent of an active ingredient selected from the group consisting of valproic acid, a pharmaceutically acceptable salt or ester of valproic acid, divalproex sodium, and valpromide; from about 20 weight percent to about 40 weight percent hydroxypropyl methylcellulose; from about 5 weight percent to about 15 weight percent lactose, from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 weight percent to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 microns; all weight percentages based upon the total weight of the granular composition.

In a further embodiment, the present invention provides a granular composition suitable for pressing into a controlled release tablet dosage form comprising the steps of a) dry blending a mixture of from about 50 weight percent to about 55 weight percent divalproex sodium, from about 20 weight percent to about 40 weight percent hydroxypropyl methylcellulose, and from about 5 weight percent to about 15 weight percent lactose to form a uniform mixture of the dry ingredients; b) wet granulating the dry uniform mixture from step a); c) drying and sizing the wet granules from step b) to select granules having an average size below 1 mm; and d) dry blending the granules with from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 weight percent to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 microns, or the microcrystalline cellose can be dry blended in step (a) with the divalproex sodium, hydroxypropyl methylcellulose and lactose.

In yet another embodiment, the present invention provides a method of preparing a controlled release tablet dosage form of divalproex sodium comprising the steps of a) dry blending a mixture of from about 50 weight percent to about 55 weight percent divalproex sodium, from about 20 weight percent to about 35 weight percent hydroxypropylmethyl cellulose, from about 5 weight percent to about 15 weight percent lactose to form a uniform mixture of the dry ingredients; b) wet granulating the dry uniform mixture from step a); c) drying and sizing the wet granules from step b) to select granules having an average size below 1 mm; d) dry blending the granules with from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 weight percent to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 microns; and e) compressing the blended granules of step h) under a force ranging between about 2000 lbf (about 8.9×10^3 Newtons) and 10,000 lbf (about 4.45×10^4 Newtons). In a similar manner, the microcrystalline cellulose can be dry blended in step (a) with the divalproex sodium, hydroxypropyl methylcellulose and lactose.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, which form a part of this specification:

FIG. 1 is a graphical representation of the release of drug from several test controlled release tablet formulations under in vitro conditions.

FIG. 2 is a graphical representation of in vitro release of drug from two preferred controlled release tablet formulations of the invention.

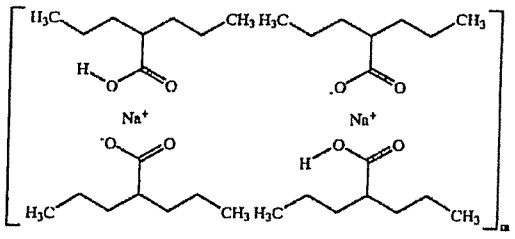
FIG. 3 is a graphical representation of plasma concentration in human subjects following administration of two of the preferred controlled release tablet formulations of the invention.

FIG. 4 is a graph showing plasma concentrations of valproic acid in a human subject following multiple administrations of a preferred controlled release formulation of the invention.

DETAILED DESCRIPTION

As used throughout this specification and the appended claims, the terms "sustained release," "prolonged release," and "controlled release" as applied to drug formulations have the meanings ascribed to them in "Remington's Pharmaceutical Sciences," 18th Ed., p. 1677, Mack Pub. Co., Easton, Pa. (1990). Sustained release drug systems include any drug delivery system which achieves the slow release of drug over an extended period of time, and include both prolonged and controlled release systems. If such a sustained release system is effective in maintaining substantially constant drug levels in the blood or target tissue, it is considered a controlled release drug delivery system. If, however, a drug delivery system is unsuccessful at achieving substantially constant blood or tissue drug levels, but nevertheless extends the duration of action of a drug over that achieved by conventional delivery, it is considered a prolonged release system.

The formulations of the present invention provide a controlled release formulation for valproic acid. The term "valproic acid" is meant to encompass the compound 2-propylpentanoic acid per se, and its pharmaceutically acceptable salts, and compounds which readily metabolize in vivo to produce valproic acid, such as valproic acid amide (valpromide), as well as other pharmaceutically acceptable amides and esters of the acid. A particularly preferred form of valproic acid for the compositions of the present invention is the complex formed between one mole of 2-propylpentanoic acid and its sodium salt, commonly referred to a "divalproex sodium." Divalproex sodium is disclosed in U.S Pat. Nos. 4,988,731 and 5,212,326 to Meade and can be represented by the following formula where m ranges from two to about six:



Experimental

One gram tablets containing 538 mg of divalproex sodium, magnesium stearate, dicalcium phosphate, microcrystalline cellulose (Avicel®, FMC Corporation, Philadelphia, Pa., USA) and/or lactose and various hydrophilic polymers were prepared. Hydrophilic polymers tested included hydroxypropyl methylcellulose, methylcellulose (Methocel® grades K100LVP CR, K4MP CR, K15MP CR and K100MP CR, Dow Chemical, Midland, Mich., USA); hydroxypropyl cellulose (Klucel® LF, Hercules, Inc., Wilmington, Del., USA); and alginate (Keltone® grades LVCR and HVCR, Kelco Co., San Diego, Calif., USA).

Bulk drug was milled prior to use and was sized to pass a 40 mesh sieve (0.42 mm nominal mesh opening). The milled and sieved bulk drug was dry-mixed with polymer and excipients in a Collette Gral 10 high shear mixer for 5

min at a high chopper speed of 3000 rpm and impeller speed of 200 rpm. Granules were prepared by adding 70 ml/kg of granulation fluid (water or water/ethanol mixtures) to the polymer/drug/excipient powder mixture over a 1–2 minute period at high chopper speed of 3000 rpm and impeller speed of 500 rpm. Additional fluid of 10–165 ml was added in one step as needed in order to reach granulation end-point. Total granulation time ranged from 2–18 min.

Tablet matrix ingredients included microcrystalline cellulose, lactose, magnesium stearate, and silicon dioxide. The resulting granules were tray dried at 50° C.–55° C. overnight under reduced pressure. The dried granules were mixed with lubricant (magnesium stearate) in a bag and then passed through a 20 mesh (0.84 mm nominal opening) sieve. Tablets weighing 1 g were pressed in a Model C Carver Press tableting machine using a 0.747 inch (1.9 cm)×0.360 inch (0.91 cm) ovaloid die at a compression force between about 2000 lbf (about 8.9×10^3 Newtons) and about 10,000 lbf (about 4.45×10^4 Newtons), preferably between about 2300 lbf (1.02×10^4 Newtons) to about 5000 lbf (2.25×10^4 Newtons). The tablet compositions are presented in Table 1.

TABLE 1

Test Divalproex Matrix Tablet Formulations

Ingredient[1]	A	B	C	D	E	F	G	H	I
Divalproex sodium	50	50	50	50	50	53.8	53.8	53.8	53.8
Methocel® K100LVPCR	18	20	—	—	—	—	—	—	10
Methocel® K4MPCR	8	—	—	—	—	—	—	—	—
Klucel® LF	—	20	—	—	—	—	—	—	—
Keltone® HVCR	—	—	30	—	—	—	—	—	—
Methocel® K15MPCR	—	—	—	—	30	26	35	—	16
Methocel® K100MPCR	—	—	—	15	—	—	—	30	—
Lactose	23	9.5	9.5	29.5	14.5	14.7	5.7	10.7	14.7
Avicel® PH101	—	0	5	5	5	5	5	5	5
PVP[2]	—	—	5	—	—	—	—	—	—
Magnesium Stearate	1	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

[1]Percent by weight, based upon the total tablet weight
[2]Poly(vinylpyrrolidone)

Initial Formulation Screening

Initial screening of the matrix tablet formulations was performed using a number of tests. Tablet hardness for each formulation was measured using a Model VK2000 VanKel tablet hardness analyzer and recorded in units of kiloPascals (kP) as the average of ten trials.

Friability of the tablets were tested by rotating the tablets samples 100 times using a Erweka TA friabilator. Friability of tablets for each formulation were calculated based on the weight loss of the tablets in this test.

Bulk density of the formulation granules was measured by carefully filling a glass graduated cylinder to the 100 ml mark. Tap density was determined following 100 taps of the filled cylinder.

Determination of granule size distribution was performed by collecting granules larger than 140 mesh (about 0.105 mm nominal mesh opening) and 40 mesh (about 0.42 mm nominal mesh opening) for evaluation of the percentage of fines and large granules.

In vitro dissolution tests were conducted using Apparatus II described in the United State Pharmacopeia XXI/National Formulary XVI. Samples aliquots of 1.5 ml were withdrawn and filtered through a 0.45 μm filter and assayed by TDX® fluorescent polarization immunoassay. Upon withdrawal of each sample, an equal volume of medium was added to the test mixture to maintain constant volume. The test conditions were as follows:

Apparatus	USP II, paddle
Medium	1M HCl for one hour; remaining time pH 6.8 buffer
Volume of medium	900 ml
Temperature	37° C. ± 0.5° C.
Paddle speed	100 rpm
Sampling volume	1.5 ml
Sampling times	0, 0.5, 1, 2, 4, 6, 8, 13, 24 hours

The results of these tests are presented in Table 2.

Based upon these initial studies, and the data appearing in Table 2 above, the following conclusions were drawn:

(1) Effects on tablet hardness: The use of ethanol as a granulation fluid tends to increase tablet hardness. There is a strong interaction between ethanol and particle size of the bulk drug. The increase in hardness was only observed for formulations containing drug of larger particle size. The opposite effect was found for drug of smaller particle size.

(2) Effects on friability: The use of drug having a small particle size reduced friability. However, this effect was significant only for formulations using water as granulation fluid.

(3) Effects on density: The use of ethanol as a granulation fluid was shown to decrease the density of the granules. However, significant interactions of ethanol with the use of Klucel®, and of ethanol with drug particle size were observed. Ethanol decreased the density only of formulations containing drug of larger particle size and/or formulations without Klucel® present. The opposite effects were found for formulations containing smaller drug particles and/or Klucel®. The same conclusions were obtained with either tap or bulk density as response.

(4) Effects on size of granules: More granules of larger size were obtained with the use of drug having a larger particle size. Moreover, interaction between ethanol and Klucel® was found to be significant i.e. use of ethanol tends to generate larger granules when there is no Klucel® present in the formulation. No effect was observed for formulations containing 4% Klucel®. Factors that showed significant influences on the percentage of fines in the granules included ethanol, drug particle size, and their interaction. Using smaller drug particles tended to yield more fines in the granules. More fines were generated when ethanol was used as a granulation fluid. The effect of ethanol was most significant for formulations containing drug of a small particle size.

(5) Effects on granulation fluid volume: In order to obtain granulation end-point, more fluid volume was needed for formulations containing either drug of a smaller particle size or with the use of ethanol as granulation fluid.

(6) In vitro drug release: In vitro percent release of valproic acid from controlled-release tablets are shown in FIG. 1. The difference in release profiles among formulations was small. In the study, percent release at 8 hours ($Q_{8\ hr}$) was used to represent release rate for data analysis. It was found that the use of Klucel® or drug of a larger particle size in the formulation resulted in an increase in release rate. Similar results were obtained when $Q_{10\ hr}$ or $Q_{24\ hr}$ was used to estimate the release rate.

Formulations containing high load and high viscosity grades of polymers often showed poor compressibility. This is believed to be the result of the increase in polymer order and elasticity with increasing molecular weight. Hardness of the tablets remained almost unchanged under compression forces ranging from about 3000 lb (1.3×10^4 Newtons) to about 10,000 lb (4.45×10^4 Newtons).

TABLE 2

Formulation	Granulating Fluid Volume	Hardness (kP)	Friability (% Loss)	Tap Density (g/ml)	Bulk Density (g/ml)	% Granule Size >40 Mesh	Fines[1]	$Q_{8\ hr}$ (%)[2]
A	100	11.9	0.049	0.504	0.429	22.6	6.1	27.6
B	80	7.2	0.16	0.515	0.438	31.3	9.8	29.0
C	115	12.2	0.025	0.459	0.39	30.2	3.3	28.6
D	80	8.4	0.162	0.459	0.406	38.2	6.6	30.4
E	235	10.4	0.060	0.599	0.509	21.5	40.7	27.0
F	110	12.2	0.006	0.400	0.340	49.2	1.8	28.0
G	200	9.4	0.085	0.596	0.506	24.0	29.7	29.7
H	150	12.9	0.142	0.593	0.504	35.0	22.8	30.0
I	130	9.5	0.015	0.475	0.404	33.8	1.2	28.8

[1]Defined as percent granules passing a 0.105 mm nominal mesh opening
[2]Defined as percent drug released in an 8-hour period under the in vitro test conditions

In order to increase the hardness of tablets, microcrystalline cellulose and colloidal silicon dioxide were tested by eternally adding small amounts to the granules at levels of 1–5%. Table 3 shows the results from the test. It was found that external addition of small amounts of microcrystalline cellulose or colloidal silicon dioxide significantly increased tablet hardness.

TABLE 3

Effect of External Addition of Microcrystalline Cellulose or Silicon Dioxide

Hardness Test Formulation	Additive	Hardness (kP)
Ia	None	6.2
Ib	5% Avicel ®	9.6
Ic	5% Avicel ® and 1% silicon dioxide[1]	13.8
IIa	None	—
IIb	1% Silicon dioxide[1]	10.9
IIc	5% Avicel ® and 1% silicon dioxide[1]	14.4
IIIa	None	5.8
IIIb	1% Silicon dioxide[1]	10.8
IIIc	5% Avicel ® and 1% silicon dioxide[1]	14.8

[1]Silicon dioxide was Cab-O-Sil M-5 fumed silica (Cabot Corp., Boyertown, PA, U.S.A.) having average particle size of between about 0.2 and 0.3 microns

As shown by the data in Table 3, the addition of either 1% silicon dioxide or 5% microcrystalline cellulose to the hydrophilic matrix formulations of the invention almost doubled tablet hardness, while adding both resulted in a greater than doubling of tablet hardness. However, although the results shown above demonstrated improvement of tablet hardness by the combined use of the external addition of Avicel® microcrystalline cellulose and Cab-o-Sil® silicon dioxide, problems of sticking and relatively low density persisted. The low bulk density (i.e. 40 g/l) of the small particle size Cab-O-Sil® fumed silica led to the problem of not being able to load sufficient material into the tablet die.

In response to this problem, a different silicon dioxide having a larger average particle size ranging from about 1 micron to about 10 microns, preferably ranging between about 2 microns to about 5 microns, and most preferably about 2–3 microns was used. One such material is available as Syloid® 244, available from W. R. Grace, Lexington, Mass., USA. When this material was used, initially intended as a de-tackifying and hardening agent for tableting, a surprising and unexpected benefit was conferred upon the formulation, as shown below. The material was added "externally" to the formulation: that is, the active ingredient, polymer(s) and excipients were dry blended, wet granulated, and then dried and sized. The silicon dioxide was then added to the granular formulation and the resulting mixture blended prior to pressing into tablets.

On the basis of the above findings, preferred tablet formulations were chosen for an in vivo absorption study in healthy human subjects. The ingredients of the formulations and in vitro release rates are shown in Table 4 and FIG. 2, respectively. The formulations were designed to have different release rates by using high viscosity HPMC alone or blended with low viscosity HPMC. The target in vitro release rates were chosen to release drug in vivo for 16–20 hours.

Using the two preferred formulations described in Table 4, two in vivo studies in human subjects were carried out. FIG. 3 shows the mean plasma concentration-time profiles of valproic acid in humans following a single oral dose of the two formulations. It was found that preferred formulations A and B provided prolonged absorption of valproic acid for approximately 10 hours and 24 hours respectively. It was apparent that the slower releasing formulation, tablet B, showed more desirable sustained plasma levels. Therefore, this formulation was further tested in a multiple dose study in healthy human subjects at an oral dose of 1 gram given once daily. The results shown in FIG. 4 indicated that mean steady-state plasma levels were well controlled between 62.3 and 78.2 μg/ml with minimal fluctuation, which falls within the therapeutic range of valproic acid (30–100 μg/ml).

TABLE 4

Preferred Controlled Release Formulations of the Invention

Ingredient	Preferred Formulation A	Preferred Formulation B
Divalproex sodium (milled)[1]	53.82%[2]	53.82%
Hydroxypropyl methylcellulose (Methocel ® K15M, CR)	8%	30%
Methyl cellulose (Methocel ® K100L, CR)	18%	—
Anhydrous lactose	12.18%	8.18%

TABLE 4-continued

Preferred Controlled Release Formulations of the Invention

Ingredient	Preferred Formulation A	Preferred Formulation B
Microcrystalline cellulose (Avicel ® PH 101)	5%	5%
Silicon dioxide (Average particle size 1 μm< >10 μm) (Syloid ® 244)	3%	3%
Total tablet weight	1 g	1 g

[1]Bulk drug sized to pass a 40 mesh sieve (0.42 mm nominal mesh opening

[2]All percentages in the Table expressed as weight percentages based upon the total weight of the tablet

The controlled release tablet formulations of the present invention thus provide an effective delivery system for the once daily administration of valproic acid (divalproex sodium) to patients in need of such treatment. The formulations of the invention provide substantially level plasma concentrations of valproic acid falling within the therapeutic range of the drug over a period which permits administration once daily.

While there have been shown and described what are the preferred embodiments of the invention, one skilled in the pharmaceutical formulation art will appreciate that various modifications in the formulations and process can be made without departing from the scope of the invention as it is defined by the appended claims.

We claim:

1. A controller release tablet dosage form comprising:

a) a hydrophilic matrix formed from a uniform admixture of:

i) about 50 weight percent to about 55 weight percent of an active ingredient selected from the group consisting of valproic sodium acid, a pharmaceutically acceptable salt or ester if valproic acid, divalproex sodium, and valpromide;

ii) about 20 weight percent to about 40 weight percent of hydroxypropyl methylcellulose, and

iii) about 5 weight percent to about 15 weight percent of lactose;

b) from about 4 weight percent to about 6 weight percent of microcrystalline cellulose;

c) and from about 1 about 5 weight percent of silicon dioxide;

all weight percentages are based upon the total weight of the tablet dosage form.

2. A controlled release tablet dosage form according to claim 1 wherein said active ingredient is divalproex sodium.

3. A controlled release tablet dosage form according to claim 1 wherein said hydroxypropyl methylcellulose is present in an amount of between about 20 weight percent and about 35 weight percent, based on the total weight of the tablet dosage form.

4. A controlled release tablet dosage form according to claim 1 wherein said silicon dioxide has an average particle size ranging between about 1 micron and about 10 microns.

5. A controlled release tablet formulation comprising:

a) a hydrophilic matrix formed from a uniform admixture of about 54 weight percent divalproex sodium, about 30 weight percent hydroxypropyl methylcellulose, and about 8 weight percent lactose;

b) about 5 weight percent microcrystalline cellulose, and;

c) about 3 weight percent silicon dioxide; all weight percentages are based upon the total weight of the tablet dosage form.

6. A granular composition for pressing into a controlled release tablet dosage form, having a particle size ranging between about 0.100 mm and about 0.84 mm comprising:

a) a uniform admixture of about 50 weight percent to about 55 weight percent of an active ingredient selected from the group consisting of valproic acid, a pharmaceutically acceptable salt or ester of valproic acid, divalproex sodium, and valpromide, about 20 weight percent to about 40 weight percent of hydroxypropyl methylcellulose, and about 5 weight percent to about 15 weight percent of lactose;

b) from about 4 weight percent to about 6 weight percent of microcrystalline cellulose, and

c) from about 1 to about 5 weight percent of silicon dioxide; all weight percentages based upon the total weight of the granular composition.

7. The granular composition according to claim 6 wherein said hydroxypropyl methyl cellulose is present in an amount of between about 25 weight percent and about 35 weight percent, based on the total weight of the granular composition.

8. The granular composition according to claim 6 wherein said silicon dioxide has an average particle size ranging between about 1 micron and about 10 microns.

9. A granular composition for pressing into a controlled release tablet dosage form comprising:

a) a uniform admixture of about 54 weight percent divalproex sodium, about 30 weight percent hydroxypropyl methylcellulose, and about 8 percent lactose;

b) about 5 weight percent microcrystalline cellulose, and;

c) about 3 weight percent silicon dioxide, all weight percentages are based upon the total weight of the granular composition.

10. A granular composition for pressing into a controlled release tablet dosage form comprising about 54 weight percent divalproex sodium, about 30 weight percent hydroxypropyl methylcellulose, about 8 weight percent lactose, about 5 weight percent microcrystalline cellulose, and about 3 weight percent silicon dioxide having an average particle size ranging from about microns to about 2 microns to about 5 microns.

11. A method of preparing a granular composition suitable for pressing into a controlled release tablet dosage form comprising the steps of:

a) dry blending a mixture of from about 50 weight percent to about 55 weight percent divalproex sodium, from about 20 weight percent to about 40 weight percent hydroxypropyl methylcellulose, and from about 5 weight percent to about 15 weight percent lactose to from a uniform mixture of the dry ingredients;

b) wet granulating the dry uniform mixture from step a);

c) drying and sizing the wet granules from step b) to select granules having an average size below about 0.84 mm; and

d) dry blending the granules with from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 micron.

12. A method of preparing a controlled release tablet dosage form of divalproex sodium comprising the steps of:

a) milling bulk divalproex sodium and sizing it to have an average particle size less than about 0.5 mm;

b) dry blending a mixture of from about 50 weight percent to about 55 weight percent divalproex sodium, from about 20 weight percent to about 35 weight percent hydroxypropyl methylcellulose, and from about 5 weight percent to about 15 weight percent lactose form a uniform mixture of the dry ingredients;

c) wet granulating the dry uniform mixture from step a);

d) drying and sizing the wet granules from step b) to select granules having an average size below 1 mm; and

e) dry blending the granules with from about 4 weight percent to about 6 weight percent microcrystalline cellulose, and from about 1 to about 5 weight percent silicon dioxide having an average particle size ranging between about 1 micron and about 10 micron; and

f) compressing the blended granules of step e) under a force ranging between about 2000 lbf and about 10,000 lbf.

13. The method of claim **12** wherein said silicon dioxide has an average particle size ranging between about 2 microns and about 5 microns.

14. A method of treating epilepsy comprising administering once daily to a patient in need of such treatment a controlled release tablet dosage form according to claim **1**.

15. A method of treating epilepsy comprising administering once daily to a patient in need of such treatment a controlled release tablet dosage form according to claim **2**.

16. A method of treating epilepsy comprising administering once daily to a patient in need of such treatment a controlled release tablet dosage form according to claim **5**.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,419,953 B1
DATED : July 16, 2002
INVENTOR(S) : Yihong Qiu et al.

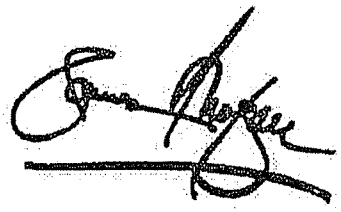
It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title page,
Item [75], Inventors, replace "**Paul Richard Poska**" with -- **Richard Paul Poska** --.

Column 12,
Line 1, replace "e" with -- h --.

Signed and Sealed this

Fourth Day of November, 2003



JAMES E. ROGAN
Director of the United States Patent and Trademark Office

JS 44 (Rev. 11/04)

CIVIL COVER SHEET

The JS 44 civil cover sheet and the information contained herein neither replace nor supplement the filing and service of pleadings or other papers as required by law, except as provided by local rules of court. This form, approved by the Judicial Conference of the United States in September 1974, is required for the use of the Clerk of Court for the purpose of initiating the civil docket sheet. (SEE INSTRUCTIONS ON THE REVERSE OF THE FORM.)

I. (a) PLAINTIFFS

ABBOTT LABORATORIES

(b) County of Residence of First Listed Plaintiff Lake County, IL
(EXCEPT IN U.S. PLAINTIFF CASES)

(c) Attorney's (Firm Name, Address, and Telephone Number)
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DEFENDANTS

TEVA PHARMACEUTICALS USA, INC

County of Residence of First Listed Defendant Montgomery County, PA
(IN U.S. PLAINTIFF CASES ONLY)
NOTE: IN LAND CONDEMNATION CASES, USE THE LOCATION OF THE LAND INVOLVED.

Attorneys (If Known)
Sutherland, Asbill & Brennan LLP
999 Peachtree Street, N.E.
Atlanta, GA 30309-3996 (404) 853-8000

II. BASIS OF JURISDICTION (Place an "X" in One Box Only)

- ☐ 1 U.S. Government Plaintiff
- ☒ 3 Federal Question (U.S. Government Not a Party)
- ☐ 2 U.S. Government Defendant
- ☐ 4 Diversity (Indicate Citizenship of Parties in Item III)

III. CITIZENSHIP OF PRINCIPAL PARTIES (Place an "X" in One Box for Plaintiff and One Box for Defendant)
(For Diversity Cases Only)

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Citizen of This State	☐ 1	☐ 1	Incorporated *or* Principal Place of Business In This State	☐ 4	☐ 4
Citizen of Another State	☐ 2	☐ 2	Incorporated *and* Principal Place of Business In Another State	☐ 5	☐ 5
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IV. NATURE OF SUIT (Place an "X" in One Box Only)

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- ☐ 160 Stockholders' Suits
- ☐ 190 Other Contract
- ☐ 195 Contract Product Liability
- ☐ 196 Franchise

REAL PROPERTY
- ☐ 210 Land Condemnation
- ☐ 220 Foreclosure
- ☐ 230 Rent Lease & Ejectment
- ☐ 240 Torts to Land
- ☐ 245 Tort Product Liability
- ☐ 290 All Other Real Property

TORTS

PERSONAL INJURY
- ☐ 310 Airplane
- ☐ 315 Airplane Product Liability
- ☐ 320 Assault, Libel & Slander
- ☐ 330 Federal Employers' Liability
- ☐ 340 Marine
- ☐ 345 Marine Product Liability
- ☐ 350 Motor Vehicle
- ☐ 355 Motor Vehicle Product Liability
- ☐ 360 Other Personal Injury

PERSONAL INJURY
- ☐ 362 Personal Injury - Med. Malpractice
- ☐ 365 Personal Injury - Product Liability
- ☐ 368 Asbestos Personal Injury Product Liability

PERSONAL PROPERTY
- ☐ 370 Other Fraud
- ☐ 371 Truth in Lending
- ☐ 380 Other Personal Property Damage
- ☐ 385 Property Damage Product Liability

CIVIL RIGHTS
- ☐ 441 Voting
- ☐ 442 Employment
- ☐ 443 Housing/ Accommodations
- ☐ 444 Welfare
- ☐ 445 Amer. w/Disabilities - Employment
- ☐ 446 Amer. w/Disabilities - Other
- ☐ 440 Other Civil Rights

PRISONER PETITIONS
- ☐ 510 Motions to Vacate Sentence

Habeas Corpus:
- ☐ 530 General
- ☐ 535 Death Penalty
- ☐ 540 Mandamus & Other
- ☐ 550 Civil Rights
- ☐ 555 Prison Condition

FORFEITURE/PENALTY
- ☐ 610 Agriculture
- ☐ 620 Other Food & Drug
- ☐ 625 Drug Related Seizure of Property 21 USC 881
- ☐ 630 Liquor Laws
- ☐ 640 R.R. & Truck
- ☐ 650 Airline Regs.
- ☐ 660 Occupational Safety/Health
- ☐ 690 Other

LABOR
- ☐ 710 Fair Labor Standards Act
- ☐ 720 Labor/Mgmt. Relations
- ☐ 730 Labor/Mgmt.Reporting & Disclosure Act
- ☐ 740 Railway Labor Act
- ☐ 790 Other Labor Litigation
- ☐ 791 Empl. Ret. Inc. Security Act

BANKRUPTCY
- ☐ 422 Appeal 28 USC 158
- ☐ 423 Withdrawal 28 USC 157

PROPERTY RIGHTS
- ☐ 820 Copyrights
- ☒ 830 Patent
- ☐ 840 Trademark

SOCIAL SECURITY
- ☐ 861 HIA (1395ff)
- ☐ 862 Black Lung (923)
- ☐ 863 DIWC/DIWW (405(g))
- ☐ 864 SSID Title XVI
- ☐ 865 RSI (405(g))

FEDERAL TAX SUITS
- ☐ 870 Taxes (U.S. Plaintiff or Defendant)
- ☐ 871 IRS—Third Party 26 USC 7609

OTHER STATUTES
- ☐ 400 State Reapportionment
- ☐ 410 Antitrust
- ☐ 430 Banks and Banking
- ☐ 450 Commerce
- ☐ 460 Deportation
- ☐ 470 Racketeer Influenced and Corrupt Organizations
- ☐ 480 Consumer Credit
- ☐ 490 Cable/Sat TV
- ☐ 810 Selective Service
- ☐ 850 Securities/Commodities/ Exchange
- ☐ 875 Customer Challenge 12 USC 3410
- ☐ 890 Other Statutory Actions
- ☐ 891 Agricultural Acts
- ☐ 892 Economic Stabilization Act
- ☐ 893 Environmental Matters
- ☐ 894 Energy Allocation Act
- ☐ 895 Freedom of Information Act
- ☐ 900Appeal of Fee Determination Under Equal Access to Justice
- ☐ 950 Constitutionality of State Statutes

V. ORIGIN (Place an "X" in One Box Only)

☒ 1 Original Proceeding ☐ 2 Removed from State Court ☐ 3 Remanded from Appellate Court ☐ 4 Reinstated or Reopened ☐ 5 Transferred from another district (specify) ☐ 6 Multidistrict Litigation ☐ 7 Appeal to District Judge from Magistrate Judgment

VI. CAUSE OF ACTION

Cite the U.S. Civil Statute under which you are filing (**Do not cite jurisdictional statutes unless diversity**):
35 U.S.C. §271(e)(2)

Brief description of cause:
Patent infringement action under the Hatch-Waxman Act.

VII. REQUESTED IN COMPLAINT:

☐ CHECK IF THIS IS A CLASS ACTION UNDER F.R.C.P. 23

DEMAND $

CHECK YES only if demanded in complaint:
JURY DEMAND: ☐ Yes ☒ No

VIII. RELATED CASE(S) IF ANY (See instructions): JUDGE _____ DOCKET NUMBER _____

DATE
May 4, 2007

SIGNATURE OF ATTORNEY OF RECORD

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RECEIPT # _____ AMOUNT _____ APPLYING IFP _____ JUDGE _____ MAG. JUDGE _____

AO FORM 85 RECEIPT (REV. 9/04)

United States District Court for the District of Delaware

Civil Action No. 07-250

ACKNOWLEDGMENT OF RECEIPT FOR AO FORM 85

NOTICE OF AVAILABILITY OF A UNITED STATES MAGISTRATE JUDGE TO EXERCISE JURISDICTION

I HEREBY ACKNOWLEDGE RECEIPT OF 1 COPIES OF AO FORM 85.

5/4/07
(Date forms issued)

(Signature of Party or their Representative)

Carl Johnson
(Printed name of Party or their Representative)

Note: Completed receipt will be filed in the Civil Action